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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,445	03/09/2001	Gary Van Nest	377882001300	7011

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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/802,445	NEST ET AL.
	Examin r	Art Unit
	Daniel M Sullivan	1636

-- The MAILING DATE of this communication appears on the cover sheet with the corr spondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7 August 2003 and 4 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,9-12,14 and 23-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,9-12,14 and 23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a response to the "AMENDMENT AND RESPONSE UNDER 37 C.F.R. §1.111" of 7 August 2003 (hereinafter 7 August Paper) and the "DECLARATION OF GARY VAN NEST, PH.D. PURSUANT TO 37 CFR §1.132" of 4 September 2003 (hereinafter, 4 September declaration) filed in reply to the Non-Final Office Action mailed 7 March 2003 (hereinafter, 7 March Office Action). Claims 1-16 were considered in the 7 March Office Action. Claims 5, 7, 8, 13, 15 and 16 were canceled, claims 1 and 9 were amended and claims 23-26 were added in the 7 August Paper. Claims 1-4, 6, 9-12, 14 and 23-26 are pending and under consideration.

Response to Amendment

Rejection of claims 5, 7, 8, 13, 15 and 16 is rendered moot by cancellation of the claims.

Claim Rejections - 35 USC § 112

Claims 1-4, 6, 9-12 and 14 stand rejected and newly added claims 23-26 are rejected under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter. The enablement rejections of record are withdrawn in part and maintained in part.

The claims are rejected because the specification, while being enabling for a method for reducing the severity of a symptom of papillomavirus infection in a human infected with papillomavirus comprising administering an immunostimulatory sequence comprising 5'-C,G, pyrimidine,pyrimidine,C,G-3', wherein a papillomavirus antigen is not administered in conjunction with administration of said immunostimulatory sequence and said

immunostimulatory sequence is administered at the site of a papillomavirus lesion, does not reasonably provide enablement for the method wherein the composition is administered prior to development of a lesion or outside of the affected area.

First, it should be pointed out that the previous Office Action was made Non-Final, in part, to clarify that the enablement rejection set forth beginning on page 5 of the Office Action mailed 24 September 2002 also applies to claims 1-4 and 6 (see the 7 March Office Action, page 2, first sentence of the final paragraph).

In response to the rejection and arguments of record, Applicant has filed a Rule 1.132 declaration, which Applicant asserts to provide experimental results demonstrating that both local and systemic administration of ISS-containing polynucleotides leads to regression of papilloma lesions. The showings provided have been fully considered but are not deemed probative.

The declaration describes experiments wherein rabbits were inoculated with CRPV-mE8 DNA at three sites on the left side and three sites on the right side of the animal. Once papillomavirus lesions had developed, the left side papillomas were treated with ISS or PBS. Importantly, "all treatments were delivered intralesionally into the base of the papilloma" (4 September declaration, paragraph 8). The findings show regression of both locally treated (i.e., left side) and systemically treated (i.e., right side) papillomas. However, because ISS was administered, in all cases, at the site of a papillomavirus lesion, the experiments described in the declaration do not test whether administration of ISS prior to the development of a lesion or away from the site of papillomavirus infection can delay the development of, or reduce the severity of a symptom of papillomavirus infection. Instead, the experiments demonstrate that

administration of ISS at the site of one lesion can effect regression of an untreated lesion in the same animal. Such an effect is not beyond what has been acknowledged to be the enabled scope of the invention.

In the first paragraph on page 9, Applicant points out that ISS-containing polynucleotides are known to stimulate innate immunity and therefore ISS-containing polynucleotides have immunostimulatory activity outside of the presence of antigen and thus, an antigen source is not required for immunostimulatory activity. Applicant's point is taken; however, the instant claims are not directed to eliciting immunostimulatory activity. The claims are directed to a method of delaying the development of a symptom or reducing the severity of a symptom of papillomavirus infection. Regardless of whether innate immunity is activated, the skilled artisan would not expect that administration of ISS away from or prior to the development of a papillomavirus lesion would be capable of delaying development of or reducing the severity of a symptom of papillomavirus infection given the teachings from the prior art and instant specification cited in the 24 September 2002 Office Action and reiterated in the paragraph bridging pages 4-6 of the 7 March Office Action. To summarize, Weiner *et al.* teaches that ISS exerts much of its adjuvant effect locally and experiments described in the instant specification clearly show that administration of ISS prior to development of a lesion has no effect on the onset or severity of disease (see especially Examples 1 and 2, and Figure 2, panels A and C).

Finally, Applicant cites findings in the art which demonstrate that administration of ISS without antigen results in a relatively long-lived resistance to *L. monocytogenes* and *F. tualrensis* bacteria, and findings in a commonly-owned pending application which demonstrate that intraperitoneal injection of ISS can treat a symptom of herpes infection. These findings have

been fully considered but are not deemed probative because *L. monocytogenes*, *F. tularensis* and herpes virus are not recognized as models of papillomavirus infection. In contrast, the instant specification describes experiments performed with an art recognized model of papillomavirus infection which clearly demonstrate that administration of ISS prior to development of a lesion has no effect on the onset or severity of disease.

Applicant's arguments have been fully considered but are not deemed persuasive either individually or as a whole. Therefore, the claims stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement for the full scope of the claimed subject matter.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Please note: Art Unit 1636 will be moving to the new USPTO facilities on 14 January 2004. After that date, Examiner Sullivan can be reached at 571-272-0779 and Examiner Yucel can be reached at 571-272-0781.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

DMS